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Comparison of prostaglandin analogue, beta-blockers and prostaglandin analogue/beta-blockers fixed combination in patients with primary open-angle glaucoma

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Summary
Purpose To compare intraocular pressure (IOP)-lowering efficacy of prostaglandin analogue, beta-blocker and prostaglandin analogue/beta-blocker fixed combination ophthalmic solution in patients with open-angle glaucoma.

Methods In this prospective, multicentre, randomized clinical trial, 120 qualifying patients received prostaglandin/beta-blocker once daily ($n=40$), prostaglandin analogue once daily in the evening ($n=40$) or beta-blocker twice daily ($n=40$). Efficacy was compared across treatment groups over 1 year.

Results Mean IOP at the first visit in the prostaglandin group was 26.6 mmHg (SD±2.0 mmHg), in beta-blockers group was 25.9 mmHg (SD±1.7 mmHg) and in prostaglandin/beta-blockers group was 26.3 mmHg (SD±2.0 mmHg). Mean IOP at the seventh visit (after 1 year) in the prostaglandin group was 19.8 mmHg (SD±1.3 mmHg), in beta-blockers group was 21.3 mmHg (SD±1.2 mmHg) and in prostaglandin/beta-blockers group was 18.4 mmHg (SD±1.3 mmHg; range: 16.0–21.0 mmHg). There was no statistically significant difference of IOP in both eyes on seventh visit by groups (KW=113.0, $p<0.0001$).

Conclusions Over 1 year of treatment, prostaglandin analogue/beta-blockers produced clinically relevant IOP reductions in patients with open-angle glaucoma that were greater than those produced by either prostaglandin analogue or beta-blockers alone. Prostaglandin analogue/beta-blocker provides both more effective IOP reduction than its components and the benefits of once-daily dosing.

Keywords Intraocular pressure (IOP) · Fixed combination · Open-angle glaucoma · Prostaglandin analogue · Beta-blockers

Vergleich eines Prostaglandinanalogon, eines Beta-Blockers und eines Kombinationspräparates von beiden in der Anwendung bei Patienten mit primärem Offenwinkelglaukom

Zusammenfassung Vergleich der Wirksamkeit zur Augendrucksenkung eines Prostaglandinanalogons, eines Beta-Blockers und eines Kombinationspräparates in der Anwendung bei primärem Offenwinkelglaukom.

Schlüsselwörter Augeninnendruck (IOP) · Kombinationspräparat · Offenwinkelglaukom · Prostaglandinanalogon · Beta-Blocker

Introduction

The term glaucoma covers a group of chronic optical neuropathies in which ganglion cell damage is associated with a loss of visual field [1]. Many patients with ocular hypertension will develop glaucoma [2–4]. Axonal loss is manifested as progressive thinning of the optic nerve head's neuroretinal rim, producing the characteristic cupping of the nerve. If untreated or inadequately treated, glaucoma can lead to blindness.

The prevalence of open-angle glaucoma has recently been estimated at 1.9 % in Americans aged >40 years [5]. This prevalence equates to approximately 2.2 million affected individuals in the United States in 2004, with an anticipated increase to 3.3 million by the year 2020 [6].

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Worldwide, there will be an estimated 60.5 million people with glaucoma by 2010 and 79.6 million by 2020. Nearly half of all worldwide glaucoma will occur in Asians (47 %), and open-angle glaucoma will account for 74 % of all glaucoma by 2020; by 2010, 4.5 million people worldwide will suffer bilateral blindness from open-angle glaucoma; this number will increase to 5.9 million by 2020 [7].

The goal of treatment in glaucoma and ocular hypertension is to reduce intraocular pressure (IOP) to a target pressure sufficiently low to prevent glaucomatous progression.

As an alternative, a number of different drugs have become available over the past 3 decades; the beta-blocker timolol was introduced in the late 1970s [8]. Topical beta-adrenergic blocking agents, such as a timolol, have been widely accepted as a first-line therapy for glaucoma and ocular hypertension [9, 10]. Beta-blockers reduce IOP by slowing the rate of aqueous humor formation [11].

Prostaglandin analogues were introduced in the late 1990s [12] and have proved to be more effective at lowering IOP than beta-blockers [13, 14]. In October 2006, one combination was approved: travoprost/timolol (travoprost 40 μg and timolol 5 mg/mL). In recent years, a new family of drugs, the prostaglandin analogues, has become mostly prescribed. Studies have shown that 0.004 % ophthalmic solution of travoprost is a potent FP receptor agonist in human ciliary muscle and trabecular meshwork cells [15, 16]. Unlike beta-blockers, prostaglandin analogues reduce IOP by increasing both uveoscleral and conventional aqueous humor outflow [17]. Travoprost is a prostaglandin analogue product approved for once-daily dosing in patients with open-angle glaucoma or ocular hypertension.

Materials and methods

Patients were eligible for participation in the study if they met the following inclusion criteria: primary open-angle glaucoma (POAG; IOP: 21 mmHg at baseline) without pseudoexfoliative or pigmentary glaucoma, 18 years of age, one ethnic group (all Caucasian) and previously not treated with any antiglaucoma medications. Exclusion criteria were known contraindications to any of the study treatments, use of any medicine that might affect IOP, abnormal ocular conditions or symptoms preventing the patient from entering the study according to the investigator's judgment, pregnancy or lactancy and patients with systemic diseases. Patients were also excluded if they had a history of chronic or recurrent severe inflammatory eye disease; had a history of ocular trauma within the preceding 6 months or ocular infection or inflammation within the preceding 3 months; had a history of clinically significant or progressive retinal disease, other severe ocular pathology that would have precluded the administration of a topical prostaglandin analogue or severe or serious hypersensitivity to any components of the study medication; had undergone intraocular surgery within the preceding 6 months or ocular laser surgery within the preceding 3 months; or had a best-corrected visual acuity worse than 0.6, anterior chamber angle grade 1 or 2 (measured by gonioscopy), a cup-to-disc (C/D) ratio greater than 0.8 or severe central visual field loss in either eye. In addition, patients could not take part if they were taking glucocorticoids or any additional topical or systemic ocular hypotensive medication; had a history of severe, unstable or uncontrolled cardiovascular, hepatic or renal disease; or had bronchial asthma or severe chronic obstructive pulmonary disease.

In all enrolled patients, best-corrected visual acuity was more than 0.9 in both eyes, C/D ratio was more than 0.8 and anterior chamber angle grade was 3 or 4 (measured by gonioscopy). Patients were without severe central visual field defects in both eyes.

The sample was recruited from outpatients attending the "Eye Clinic" in the University Clinical Centre in Pristina (Kosovo) and Ljubljana (Slovenia). All participants signed the informed consent before any study procedures were conducted.

Patients were assigned to medical interventions at random once we tested that patients fulfilled all the selection criteria of the study.

To evaluate IOP reduction at 12 months with the three medications, it was estimated that 120 cases that met all inclusion criteria and none of the exclusion criteria should be included (40 patients in each group).

IOP was measured using Goldmann applanation tonometer for each eye between 8 a.m. and 10 a.m. at baseline (day 0) and six control visits: control 1 (after 1 day), control 2 (after 7 days), control 3 (after 1 month), control 4 (after 3 months), control 5 (after 6 months) and control 6 (after 1 year).

The Kruskal–Wallis test was used for statistical analysis. A p-value of <0.05 was considered to be statistically significant.

Results

In this study were included 120 patients with POAG, of which 66 or 55.0 % were females and 54 or 45.0 % were males. Patients included in the research were divided into three groups: (1) prostaglandin group, (2) beta-blockers group and (3) prostaglandin/beta-blockers group. In each group were 40 patients. By gender, in beta-blockers group, in the structure, females were in high level, but with χ^2 test, there was no statistically significant difference between the genders ($\chi^2=2.77$, $p=0.251$, so $p>0.05$). The mean age of patients in prostaglandin group was 64.1 years (SD ± 10.7 years; range: 41–87 years). The mean age of patients in beta-blockers group was 64.9 years (SD ± 10.2 years; range: 43–82 years). The mean age of patients in prostaglandin/beta-blockers group was 58.6 years (SD ± 11.3 years; range: 36–85 years). The analysis with one-way analysis of variance showed statistically

Table 1 The patients' data

Parameter	Total	Prostaglandin	Beta-blocker	Prostaglandin/ beta-blocker	*p*-value
N	120	40	40	40	
Gender [N (%)]					
Male	54 (45.0)	21 (52.5)	14 (35.0)	19 (47.5)	0.251
Female	66 (55.0)	19 (47.5)	26 (65.0)	21 (52.5)	
Age [years (mean± standard deviation)]	62.5±11.0	64.1±10.7	64.9±10.2	58.6±11.3	0.0003

significant difference between the mean age by groups (T-test=0.567, p=0.0003, so p<0.001; Table 1).

Mean IOP at the first visit in the prostaglandin group was 26.6 mmHg (SD±2.0 mmHg), in beta-blockers group was 25.9 mmHg (SD±1.7 mmHg) and prostaglandin/beta-blockers group was 26.3 mmHg (SD±2.0 mmHg). With Kruskal–Wallis test, there was no statistically significant difference in IOP of both eyes on first visit by groups (KW=5.48, p=0.064). Mean IOP at the second visit (after 2 days) in the prostaglandin group was 22.8 mmHg (SD±1.7 mmHg), in beta-blockers group was 23.2 mmHg (SD±1.5 mmHg) and prostaglandin/beta-blockers group was 22.5 mmHg (SD±1.8 mmHg). With Kruskal–Wallis test, there was no statistically significant difference of IOP in both eyes on second visit by groups (KW=5.29, p=0.07). Mean IOP at the third visit (after 7 days) in the prostaglandin group was 20.4 mmHg (SD±2.0 mmHg), in beta-blockers group was 21.3 mmHg (SD±1.3 mmHg) and prostaglandin/beta-blockers group was 20.0 mmHg (SD±1.9 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP in both eyes on third visit by groups (KW=22.8, p<0.001). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy (p<0.001), and also between the groups treated with prostaglandin and beta-blockers (p<0.05). Mean IOP at the fourth visit (after 1 month) in the prostaglandin group was 18.9 mmHg (SD±1.6 mmHg), in beta-blockers group was 20.3 mmHg (SD±1.1 mmHg) and prostaglandin/beta-blockers group was 18.2 mmHg (SD±1.7 mmHg; range: 15.0–22.0 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP in both eyes on fourth visit by groups (KW=65.4, p<0.0001). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy (p<0.001), and also between the groups treated with prostaglandin and beta-blockers (p<0.0001). Mean IOP at the fifth visit (after 3 months) in the prostaglandin group was 18.4 mmHg (SD±1.5 mmHg), in beta-blockers group was 19.9 mmHg (SD±1.0 mmHg) and prostaglandin/beta-blockers group was 17.6 mmHg (SD±1.4 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP in both eyes on fifth visit by groups (KW=90.8, p<0.0001). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy (p<0.001), and also between the groups treated with prostaglandin and beta-blockers (p<0.0001). Mean IOP at the sixth visit (after 6 months) in the prostaglandin group was 19.0 mmHg (SD±1.4 mmHg), in beta-blockers group was 20.4 mmHg (SD±1.2 mmHg) and prostaglandin/beta-blockers group was 18.2 mmHg (SD±1.2 mmHg; range: 16.0–21.0 mmHg). With Kruskal–Wallis test, there is statistically significant difference of IOP in both eyes on sixth visit by groups (KW=86.2, p<0.0001). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy (p<0.001), and also between the groups treated with prostaglandin and beta-blockers (p<0.001). Mean IOP at the seventh visit (after 1 year) in the prostaglandin group was 19.8 mmHg (SD±1.3 mmHg), in beta-blockers group was 21.3 mmHg (SD±1.2 mmHg) and prostaglandin/beta-blockers group was 18.4 mmHg (SD±1.3 mmHg; range: 16.0–21.0 mmHg). With Kruskal–Wallis test, there was no statistically significant difference of IOP in both eyes on seventh visit by groups (KW=113.0, p<0.0001). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with prostaglandin and prostaglandin/beta-blockers fixed combination therapy (p<0.001), the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy (p<0.001), and also the groups treated with prostaglandin and beta-blockers (p<0.001; Table 2 and Fig. 1).

Table 2 Summary of mean IOP±standard deviation (mmHg) for patients on prostaglandin, beta-blockers or prostaglandin/beta-blockers therapy

Visit	Prostaglandin	Beta-blocker	Prostaglandin/ beta-blocker	*p*-value
Baseline	26.6±2.0	25.9±1.7	26.3±2.0	0.064
Day 2	22.8±1.7	23.2±1.5	22.5±1.8	0.070
Day 7	20.4±2.0	21.3±1.3	20.0±1.9	<0.0001
Month 1	18.9±1.6	20.3±1.1	18.2±1.7	<0.0001
Month 3	18.4±1.5	19.9±1.0	17.6±1.4	<0.0001
Month 6	19.0±1.4	20.4±1.2	18.2±1.2	<0.0001
Month 12	19.8±1.3	21.3±1.2	18.4±1.3	<0.0001

The mean difference of IOP between first and second visit in the patients of prostaglandin group was −3.8 mmHg (SD±1.3 mmHg), in the patients of

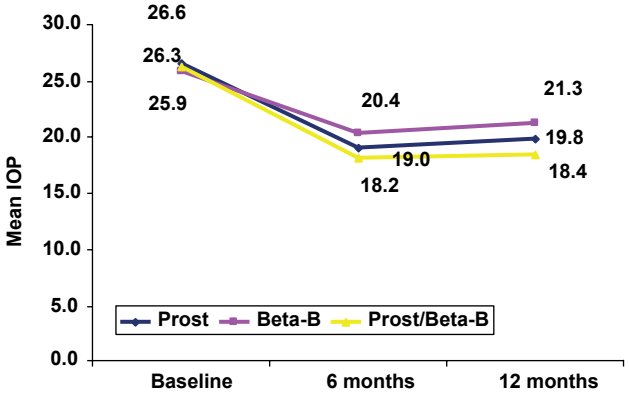

Fig. 1 Summary of mean IOP±standard deviation (mmHg) for patients on prostaglandin (Prost), beta-blockers (Beta-B) or prostaglandin/beta-blockers (Prost/Beta-B) therapy

beta-blockers group was −2.7 mmHg (SD±1.0 mmHg) and in the patients of prostaglandin/beta-blockers group was −3.8 mmHg (SD±1.4 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP value in both eyes between first and second visit by groups (KW=34.46, $p<0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$), and also between the groups treated with prostaglandin and beta-blockers ($p<0.001$). The mean difference of IOP after 6 months (from first visit) in the patients of prostaglandin group was −7.6 mmHg (SD±2.4), in the patients of beta-blockers group was −5.5 mmHg (SD±1.7) and in the patients of prostaglandin/beta-blockers group was −8.1 mmHg (SD±2.1 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP value in both eyes between first and sixth visit by groups (KW=58.9, $p<0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$), and also between the groups treated with prostaglandin and beta-blockers ($p<0.001$). The mean difference of IOP after 1 year (from first visit) in the patients of prostaglandin group was −6.8 mmHg (SD±2.2), in the patients of beta-blockers group was −4.6 mmHg (SD±1.8) and in the patients of prostaglandin/beta-blockers group was −7.9 mmHg (SD±1.9 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP value in both eyes between first and seventh visit by groups (KW=80.8, $p<0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$), the groups treated with prostaglandin and beta-blockers ($p<0.0001$) and also the groups treated with prostaglandin and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$; Table 3 and Fig. 2).

Table 3 Mean IOP±standard deviation (mmHg) change from baseline for patients on prostaglandin, beta-blockers or prostaglandin/beta-blockers therapy

Visit	Prostaglandin	Beta-blocker	Prostaglandin/beta-blocker	*p*-value
Day 2	−3.8±1.3	−2.7±1.0	−3.8±1.4	<0.0001
Day 7	−6.2±1.9	−4.6±1.5	−6.3±2.0	<0.0001
Month 1	−7.7±1.9	−5.6±1.6	−8.2±2.2	<0.0001
Month 3	−8.2±2.3	−6.0±1.8	−8.7±1.9	<0.0001
Month 6	−7.6±2.4	−5.5±1.7	−8.1±2.1	<0.0001
Month 12	−6.8±2.2	−4.6±1.8	−7.9±1.9	<0.0001

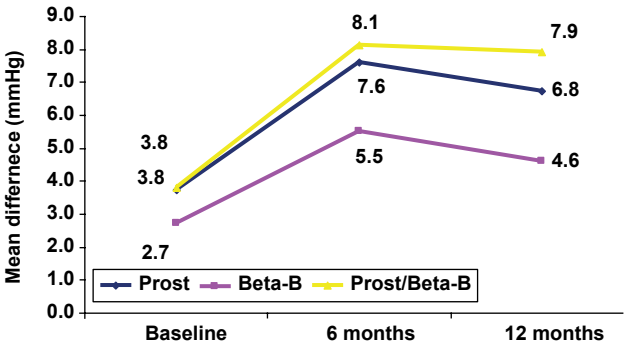

Fig. 2 Mean IOP±standard deviation (mmHg) change from baseline for patients on prostaglandin (Prost), beta-blockers (Beta-B) or prostaglandin/beta-blockers (Prost/Beta-B) therapy

The loss variance of IOP between first and second visit in the patients of prostaglandin group was 14.0% (SD±4.3%), in the patients of beta-blockers group was 10.4% (SD±3.6%) and in the patients of prostaglandin/beta-blockers group was 14.3 mmHg (SD±4.9%). With Kruskal–Wallis test, there was statistically significant difference in percentage of IOP value of both eyes between first and second visit by groups (KW=36.9, $p<0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$), and also between the groups treated with prostaglandin and beta-blockers ($p<0.001$). The loss variance of IOP after 6 months in the patients of prostaglandin group was 28.2% (SD±7.6%), in the patients of beta-blockers group was 21.1% (SD±5.5%) and in the patients of prostaglandin/beta-blockers group was 30.6% (SD±6.1%). With Kruskal–Wallis test, there was statistically significant difference in percentage of IOP value of both eyes between first and sixth visit by groups (KW=75.0, $p<0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p<0.001$), and also between the groups treated with prostaglandin and beta-blockers ($p<0.0001$). The loss variance of IOP after 1 year in the patients of prostaglandin group was 25.0% (SD±7.3%),

in the patients of beta-blockers group was 17.5 % (SD ± 6.0 %) and in the patients of prostaglandin/beta-blockers group was 29.9 % (SD ± 5.7 %). With Kruskal–Wallis test, there was statistically significant difference in percentage of IOP value of both eyes between first and seventh visit by groups (KW = 99.4, $p < 0.0001$). Dunn's multiple comparison test showed statistically significant difference of IOP value between the groups treated with beta-blockers and prostaglandin/beta-blockers fixed combination therapy ($p < 0.001$), the groups treated with prostaglandin and beta-blockers ($p < 0.0001$), and also the groups treated with prostaglandin and prostaglandin/beta-blockers fixed combination therapy ($p < 001$; Table 4 and Fig. 3).

Discussion

Although there are other risk factors associated with the development and progression of glaucoma besides IOP, the most widely studied and most important risk factor is IOP.

Prostaglandin analogues are today the most prescribed antiglaucoma monotherapy because of their potent IOP reduction and good tolerability. Approximately 40 % of patients treated for glaucoma are unable to achieve adequate control of IOP with monotherapy [3], and combination of several drugs are very common.

Table 4 Mean (%) change from baseline for patients on prostaglandin, beta-blockers or prostaglandin/beta-blockers therapy

Visit	Prostaglandin	Beta-blocker	Prostaglandin/ beta-blocker	*p*-value
Day 2	14.0 ± 4.3	10.4 ± 3.6	14.3 ± 4.9	< 0.0001
Day 7	23.0 ± 6.4	17.5 ± 5.0	23.9 ± 6.7	< 0.0001
Month 1	28.9 ± 6.9	21.4 ± 5.2	30.7 ± 7.0	< 0.0001
Month 3	30.5 ± 7.1	22.8 ± 5.4	32.9 ± 5.7	< 0.0001
Month 6	28.2 ± 7.6	21.1 ± 5.5	30.6 ± 6.1	< 0.0001
Month 12	25.0 ± 7.3	17.5 ± 6.0	29.9 ± 5.7	< 0.0001

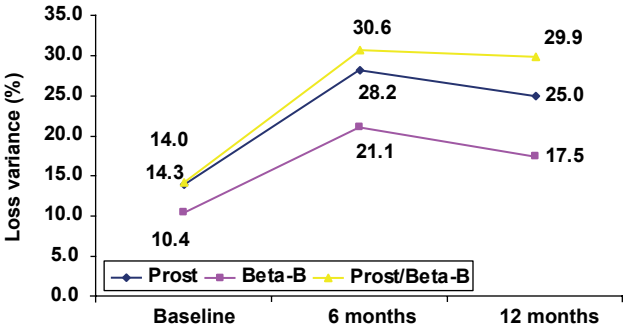

Fig. 3 Loss variance from baseline for patients on prostaglandin (Prost), beta-blockers (Beta-B) or prostaglandin/beta-blockers (Prost/Beta-B) therapy

A variety of pharmacologic therapeutic agents are currently available for the treatment of glaucoma. The aim of therapy is to lower IOP, a major causal risk factor in the progression of the disease. Topical IOP-lowering medications can delay or prevent the onset of POAG. IOP-lowering agents from different pharmacologic classes act through distinctly different mechanisms, which allow them to be used either for monotherapy or in combination. The results of the current study show that the fixed combination of travoprost/timolol produces greater IOP reductions than the positive control, timolol 0.5 %, which was administered twice daily. The fixed combination of travoprost/timolol significantly lowers IOP by 7–9 mmHg, which is a 29–33 % reduction relative to an average baseline value of 24 mmHg. In addition, the fixed combination of travoprost/timolol decreased diurnal mean IOP similarly to the concomitant travoprost or timolol therapy, with differences in mean IOP ranging from 0.4 to 1.1 mmHg. The travoprost/timolol combination lowered IOP up to 8.6 mmHg [18]. Recent studies involving the concomitant administration of beta-blockers and prostaglandin analogues have reported further reductions in IOP over those achieved with either agent dosed as a monotherapy [19].

Several clinical studies that evaluate the clinical efficacy and safety of fixed combination prostaglandin/beta-blockers have been completed, and this combination is safe and stable [20–23]. The first of these by Barnebey et al. [21] was a randomized, prospective, multicentre, double-masked, parallel group study of 263 patients with either open-angle glaucoma or ocular hypertension. After a variable washout period during which all ocular hypotensive medications were held, the patients were randomized to receive either daily (a.m) fixed-combination travoprost/timolol, with vehicle (placebo) in the evening, or twice daily timolol or daily (p.m) travoprost, with vehicle (placebo) in the morning. They were treated for a total of 3 months, while their IOP were monitored at nine different time periods. Results showed that fixed-combination travoprost/timolol lowered IOP 1.9–3.3 mmHg more that timolol alone, and 0.9–2.4 mmHg more than travoprost alone. The adverse event profile was similar among all three study arms. IOP reduction from baseline ranged 32–38 % for the fixed-combination medication, compared with 29–32 % for travoprost alone and 25–30 % for timolol alone. These results suggest that fixed-combination travoprost/timolol produced clinically relevant IOP reductions greater than either agent alone, whereas the incidence of adverse events was comparable.

Schuman et al. [20] have reported the IOP-decreasing efficacy and safety of travoprost 0.004 %/timolol maleate 0.5 % fixed combination eye drop monotherapy and those of concomitantly used travoprost 0.004 % eye drops and timolol maleate 0.5 % eye drops. This randomized, double-masked study involved administration of travoprost 0.004 %/timolol maleate 0.5 % fixed combination eye drops (155 cases) or travoprost 0.004 % with timolol 0.5 % maleate eye drops (142 cases) for patients who were

diagnosed with POAG or ocular hypertension. The range of IOP decrease was 7.3–8.3 mmHg in the group using travoprost 0.004 %/timolol maleate 0.5 % fixed combination eye drops and 6.8–8.5 mmHg in the group concomitantly using travoprost 0.004 % eye drops with timolol maleate 0.5 % eye drops; these values were not significantly different [20].

In our study, the mean IOP at the seventh visit (after 1 year) in the prostaglandin group was 19.8 mmHg (SD ± 1.3 mmHg), in beta-blockers group was 21.3 mmHg (SD ± 1.2 mmHg) and in prostaglandin/beta-blockers group was 18.4 mmHg (SD ± 1.3 mmHg; range: 16.0–21.0 mmHg). With Kruskal–Wallis test, there was no statistically significant difference of IOP in both eyes on seventh visit by groups (KW = 113.0, $p < 0.0001$). The mean difference of IOP after 1 year (from first visit) in the patients of prostaglandin group was − 6.8 mmHg (SD ± 2.2), in the patients of beta-blockers group was − 4.6 mmHg (SD ± 1.8) and in the patients of prostaglandin/beta-blockers group was − 7.9 mmHg (SD ± 1.9 mmHg). With Kruskal–Wallis test, there was statistically significant difference of IOP value in both eyes between first and seventh visit by groups (KW = 80.8, $p < 0.0001$). The loss variance of IOP after 1 year in the patients of prostaglandin group was 25.0 % (SD ± 7.3 %), in the patients of beta-blockers group was 17.5 % (SD ± 6.0 %) and in the patients of prostaglandin/beta-blockers group was 29.9 % (SD ± 5.7 %). With Kruskal–Wallis test, there was statistically significant difference in percentage of IOP value of both eyes between first and seventh visit by groups (KW = 99.4, $p < 0.0001$).

Conclusion

Well-designed observational studies can identify clinically important differences among therapeutical options and provide data on drug effectiveness and safety.

In our study, IOP-lowering effect of fixed combination prostaglandin/beta-blocker was superior in comparison with monotherapy with travoprost 0.004 % and timolol 0.5 %, with statistically significant differences in mean IOP values after 1, 3 and 6 months of therapy.

Conflict of interest

The authors declare that there are no actual or potential conflicts of interest in relation to this article.

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